What's Old is New Again: FDA issues a Draft Guidance on NCE Exclusivity Determinations for Certain Fixed-Combination Drug Products

Alan G. Minsk and Kelley C. Nduom

In the 1981 rock ballad, "Don't Stop Believin," by the band Journey, Steve Perry sings "Some will win, some will lose." The Food and Drug Administration's recently-issued draft guidance document on new chemical entity (NCE) exclusivity determinations for certain fixed-combination drug products may help identify winners and losers. This proposed new policy change, if adopted, could represent a significant departure from past agency determination and might present new exclusivity opportunities.

In the February 2014 draft guidance, "New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products," FDA discusses a potential interpretation change where, in certain cases, a drug product might be eligible to obtain five years of new chemical entity non-patent market exclusivity (sometimes referred to as "Hatch-Waxman" [or Waxman-Hatch] exclusivity), even if one of the active ingredients was previously approved by FDA.[1] Existing FDA policy has been that a fixed-combination drug product is ineligible for five years of exclusivity if it contains a previously-approved active moiety, even if the other ingredient is a new chemical entity.

FDA has provided industry sixty days to submit comments.

We will describe, very briefly, the law, the new proposed interpretation change identified in the draft guidance, and our observations. We will not detail the evolution of FDA's interpretation.

The Federal Food, Drug, and Cosmetic Act (FDC Act) states:

> If an application submitted under subsection (b) of this section for a drug [a new drug application (NDA) under section 505 of the FDC Act], no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved . . . no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section . . . .[2]

Historically, FDA has read this provision to mean that, with one limited exception (not described here), FDA will not accept the submission (i.e., it will not accept at all, not even for review) an NDA submitted under section 505(b)(2) of the FDC Act or an abbreviated new drug application that contains the same active moiety of that drug product[3] until the innovator's five-year exclusivity period expires. A company may still submit a "full" NDA (i.e., one submitted under section 505(b)(1)) during this exclusivity time.

1 See www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm386685.pdf.
2 21 U.S.C. §§ 355(j)(5)(F)(ii); 21 U.S.C. § 355(c)(3)(E)(ii).
3 FDA has interpreted "drug" in the statutory language to mean "drug product," which is defined in regulations as "a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients." See 21 C.F.R. § 314.3(b).

Highlights of New Draft Guidance

- FDA is considering interpreting the word "drug" to mean "drug substance" or "active ingredient," rather than its current view of "drug product" (i.e., final form product). The bottom line is that a five-year exclusivity determination will be made for each drug substance in a drug product, and not for the drug product as a whole.
- The new potential distinction is important; it acknowledges that many drugs with the same "drug" (i.e., substance or active ingredient) might have been previously approved alone but, if combined with an NCE, could not obtain five-year exclusivity. The financial incentive to combine an NCE with a previously-approved drug product, as it currently stands, is diminished. By potentially granting five-year exclusivity to a fixed-combination drug product, even where one ingredient has been approved, companies might become incentivized to develop such products.
- FDA notes that its new interpretation, if finalized, would only apply to prospective submissions. The agency acted, in part, in response to Citizen Petitions that challenged FDA's policy over specific products that were rejected for five-year exclusivity.

AGG Observations

- FDA's current policy remains the same (the guidance is a draft).
- Any change, if finalized, will apply only to new submissions. FDA will not retroactively award exclusivity to previously-approved fixed-combination products.
- Companies considering the development of fixed-combination products, (such as those in the cancer, cardiovascular and infectious disease areas where many products are fixed combinations) would potentially have a greater incentive to do so, if a five-year exclusivity period is possible, even if one ingredient has been previously approved. This five-year exclusivity provision can be extremely valuable due to its effective monopoly. Therefore, FDA's policy, if adopted, should make companies consider all regulatory strategies, some perhaps previously abandoned.
- FDA's new thinking represents an interesting development. While, some agency critics argue that FDA is a creature of habit and is incapable of change, here, FDA recognizes the increased usage of fixed-combination drug products and the need to incentivize companies to further develop such products. While the guidance is not final, it does reflect that FDA can (try to) change with the times.
- Some will win. Some will lose. A company may benefit if it can obtain five-year exclusivity. However, subsequent submitters might find themselves on the sidelines for five years. Time will tell if FDA makes final its policy change and who will be singing the blues.

Authors and Contributors

Alan G. Minsk
Partner, Atlanta Office
404.873.8690
alan.minsk@agg.com

Kelley C. Nduom
Associate, Atlanta Office
404.870.5796
kelley.nduom@agg.com

not *if*, but *how*.®

About Arnall Golden Gregory LLP

Arnall Golden Gregory, a law firm with more than 150 attorneys in Atlanta and Washington, DC, employs a "business sensibility" approach, developing a deep understanding of each client's industry and situation in order to find a customized, cost-sensitive solution, and then continuing to help them stay one step ahead. Selected for The National Law Journal's prestigious 2013 Midsize Hot List, the firm offers corporate, litigation and regulatory services for numerous industries, including healthcare, life sciences, global logistics and transportation, real estate, food distribution, financial services, franchising, consumer products and services, information services, energy and manufacturing. AGG subscribes to the belief "not if, but how.®" Visit www.agg.com.

Atlanta Office
171 17th Street NW
Suite 2100
Atlanta, GA 30363

Washington, DC Office
1775 Pennsylvania Ave., NW,
Suite 1000
Washington, DC 20006

To subscribe to future alerts, insights and newsletters: **http://www.agg.com/subscribe/**